NATIONAL CANCER INSTITUTE

Final Report of the Long Range Planning Committee

Translating Cancer Research into Cancer Care

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Since our first meeting in July 1998, we have worked within the Long Range Planning Committee (LRPC) to help the Director of the Office of Informatics (OI) at the National Cancer Institute (NCI) develop a vision for a new Cancer Informatics Infrastructure (CII). Our membership comes from across the nation and brings expertise in clinical trials, informatics, statistics, computer science, and medicine. At the Director's request, we have prepared this report, advising him on what he should do within the next 12 months to move this initiative forward and to serve NCI and the American public.

EXECUTIVE SUMMARY

The Long Range Planning Committee envisions a national cancer information and knowledge environment that will translate cancer research into cancer care. To this end, the Committee recommends the creation of a Cancer Informatics Infrastructure (CII) that exploits the National Information Infrastructure to speed the clinical trial process. As an "enabler," the CII will expedite information exchange, both within the National Cancer Institute and across the national cancer community.

To move the CII from theory into practice, the Committee recommends that the Office of Informatics

1. Formulate the role of the National Cancer Institute in the national standards development process.
2. Convene a national advisory meeting on oncology-related terminology and standards, focusing on the development of common data elements.
3. Focus on demonstration and evaluation projects that enhance the Institute's mission, by building on ongoing mainstream informatics initiatives and Internet technologies.
4. Develop a process to strategically and tactically diffuse the products and concepts of recommendations 1, 2, and 3 throughout the cancer community.

In 2004, the CII will support all stakeholders patients and physicians, investigators, trial managers, and payers as they make vital decisions affecting the course of cancer treatment and research. Clinical trial results will drive cancer care, and care results will drive future research.

INTRODUCTION

The goal of the Cancer Informatics Infrastructure (CII), as we envision it, is to create a national cancer information and knowledge environment that speeds the discovery process and the translation of best discoveries into clinical trials. The CII will be the "enabler" that integrates the efforts of individual researchers, clinicians and patients in ways previously impossible, given the myriad of incompatible information systems within NCI and across the national cancer community. By fostering collaboration within and beyond NCI and by exploiting the potential of

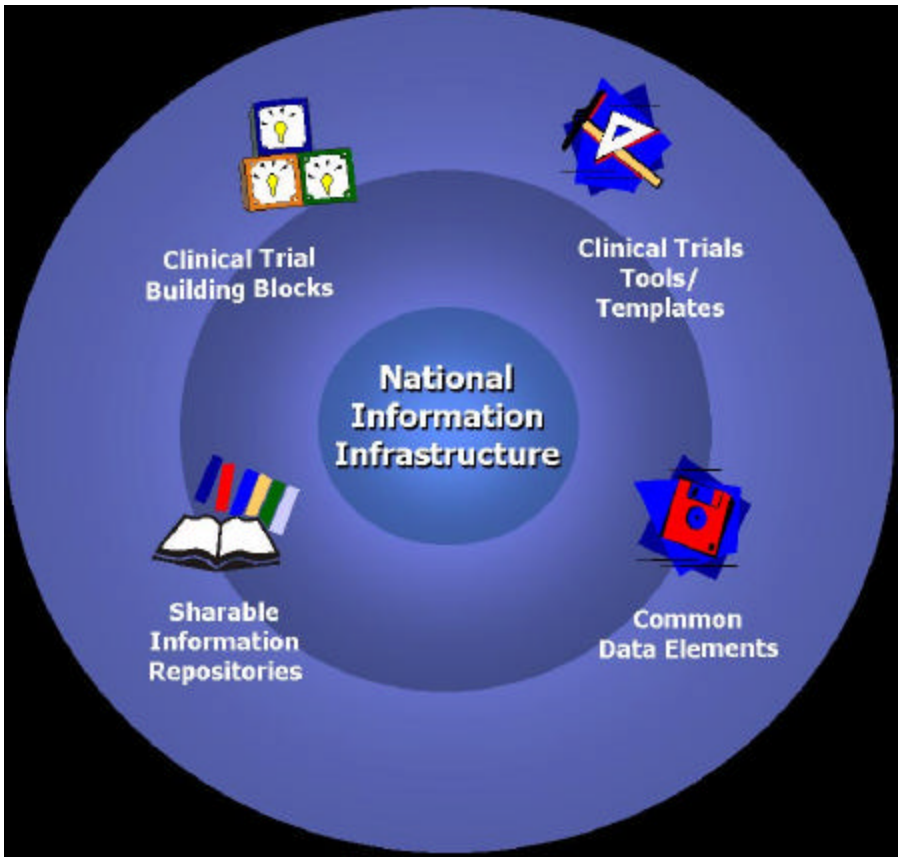
the Web, the CII will dramatically improve all aspects of cancer research and clinical care. It will expedite the process of converting the growing knowledge of genes, proteins, and pathways into the most appropriate preventative, diagnostic, and therapeutic measures.

Picturing the CII and Its New Model of the Clinical Trial Process

Our schema for the CII sets forth an architectural base for moving information across the continuum of cancer research: basic, clinical, translational, and population-based research. It is a model that brings together

- the mission, processes, and work culture of cancer research, care, and policy
- the stakeholders and "consumers" of research and care
- the tools and technologies (including hardware and software) that people use to do the work.

Figure 1: Model for the Cancer Informatics Infrastructure



With the National Information Infrastructure (NII) at its core, the CII will make maximum use of existing commercial capabilities and be poised to harvest the new technologies of the 21st Century (the inner circle shown in Figure 1). Today's Web is an essential element of the NII. It provides people with unprecedented access to online information and services. However,

because the information is unstructured, computers cannot readily "understand" it. This limitation helps explain why information on the Web is hard to find, integrate and automate. The enabling technology for the next generation Web is a new standard called XML (eXtensible Markup Language). Developed by the World Wide Web Consortium, XML makes it easy to create specialized markup languages – sets of tags that tell a computer what data means, rather than merely how to display it, as is the case with the current Web standard called HTML (HyperText Markup Language). Using XML, a number can be "understood" by the computer to be a specific laboratory result, patient history, physical finding, or patient identifier, etc. With HTML, these numbers are unstructured text that the computer does not understand.

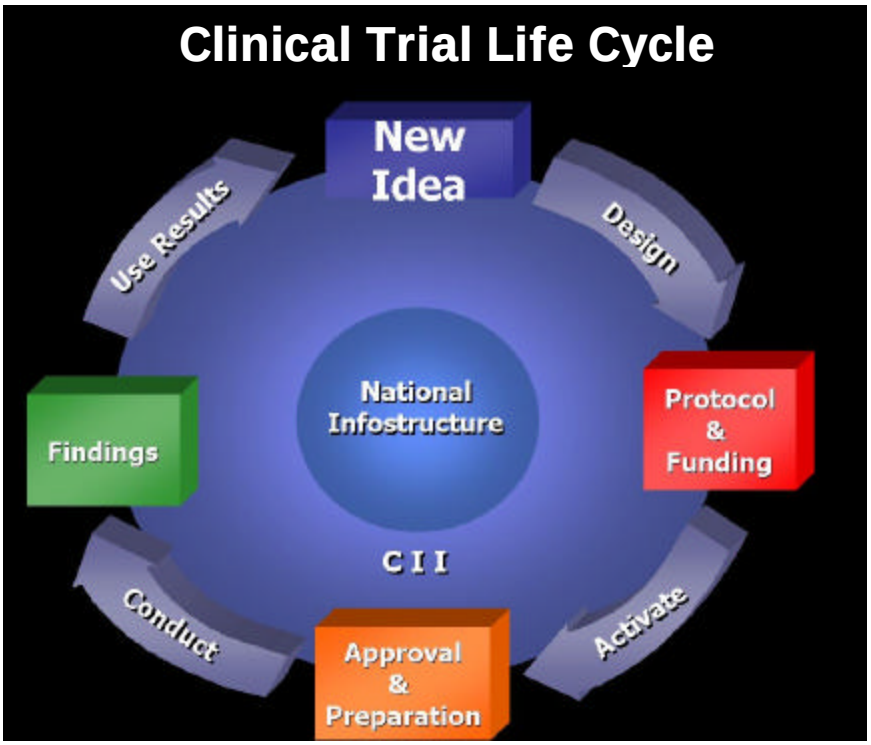
The CII will overcome these limitations by using core technologies, such as XML, to provide information and services in a structured form readily accessible to both people and computers. Sites will publish patient records, trial results, eligibility requirements, treatment schedules, and the like, so that they are available to anyone – or any Web-enabled application – with the proper authorizations. They will also publish services that enable members of the cancer community to analyze data, run disease and diagnostic models, book appointments, and so forth. Thousands of sites will build on each other's information and services, creating innovative networked medical centers and hybrid treatment protocols that accelerate the path from research to cure.

The NCI should build only those capabilities that are specific to its needs: common data elements, research building blocks, and tools to support the conduct of cancer related research. This report addresses the specific case example of how this might be implemented within the context of NCI clinical treatment and diagnostic trials. This methodology is expected to have broad application to NCI's extensive research mission from basic to applied observational, population-based research.

Although the specifics of how it might be applied to those diverse settings will need to be addressed with specific efforts, the model proposed here stresses interoperability among technologies and collaboration among communities to develop and share relevant knowledge about cancer. For NCI, this means that the CII can provide totally new ways to collaborate, such as the linkages among basic biologists, mouse researchers, genomics researchers and clinicians studying human cancers in the Mouse Models of Human Cancer Consortium. For organizations outside NCI, this means that the CII can provide links among local systems that were heretofore incompatible.

To make our vision of the CII more "real", we developed a model of what clinical research will look like in 2004. This model is presented below in this report's section on Future States. Using the CII, ideas are generated, funding and protocol approvals are obtained, clinical trials are conducted, findings are analyzed, and more new ideas are generated. The entire drug development process is greatly enhanced by eliminating redundancy, most of the paper and expediting each step. Trials are authored which focus on the science of the trial, not the text of the protocol document. They are authored collaboratively by appropriate members of the community and approved within 60 days. Patients are accrued more rapidly since clinical trials are integrated in the standard of care. The appendices contain detailed scenarios of use of our model system from the perspective of patients, physicians, investigators, trials managers and payers.

Figure 2: Clinical Trial Life Cycle



RECOMMENDATIONS

Recommendation 1. Formulate the role of the National Cancer Institute in the national standards development process.

- **Create a standing review panel for NCI information standards.** This body will peer review and seek consensus from relevant stakeholders on proposed information standards unique to the CII enterprise. Operating under one of NCI's existing advisory committees, it will liaison with other appropriate federal agencies and organizations.

- **Ensure that NCI efforts to develop or promote oncology-specific information standards are tightly coordinated with the broader health information standards community.** Coordination needs to extend to include standards development organizations (SDOs), such as HL7 and SNOMED, umbrella organizations such as ANSI HISB and ISO TC 215, and larger communities of interest such as FDA and pharmaceutical industry, NLM's UMLS, and most importantly practicing scientists and clinicians.

- **Include in the approach dynamic processes for content management and configuration control for the entire lifecycle of standards.** Content management is critical given the need to continuously revise common data elements to reflect changes

in the science. Configuration management – for example, appropriate content maintenance, version control, and seamless integration of updates – is also essential to make the implementation of standards "transparent" and as effortless as possible for cancer centers, the pharmaceutical industry, the Food and Drug Administration, and the National Cancer Institute itself.

Recommendation 2. **Convene a national advisory meeting on oncology-related terminology and standards.**

The LRPC commends the National Cancer Institute for its terminological development efforts. The implementation of the Cancer Informatics Infrastructure (CII) requires commonality, such as is provided by common toxicity criteria (CTCs). The development of common data elements (CDEs) is unique to the National Cancer Institute and critical to the CII.

We recommend that a working group be convened to consider oncology-related terminology and standards (ORTS), led by Curtis Langlotz, MD, PhD. Details of his work to date are included in the appendix on the CDE development model for spiral computed tomography in lung cancer. Assisted by Christopher Chute, MD, DrPH, other experts, and NCI staff, this working group will advise the Office of Informatics on how best to do the following:

- **Identify oncology-related terminology and standards that should be supported throughout their lifecycle by NCI.** It is critical to distinguish between oncology-relevant standards, such as SNOMED, UMLS, HL7, XML, and DICOM, and cancer-specific standards, such as CDEs and common toxicity criteria (CTCs). The ORTS working group will define the responsibility of NCI for the lifecycle of cancer-specific standards and clarify the role of NCI in the area of oncology-related standards, including appropriate linkages and participation.

- **Institute formal change management processes for CDEs and other oncology-related terminology.** As CDEs are developed and adopted, NCI will need to re-focus on monitoring adherence and providing technical assistance to support adoption and implementation for all stakeholders. Processes must ensure that terminological standards evolve in parallel with and support of clinical and research needs, including those of the pharmaceutical industry and the FDA. The ORTS working group will identify activities to
  - ✓ Develop guidelines and resource materials formalizing best practices to assist participants in CDE development
  - ✓ Elicit clinical input from designated "champions" early in each round of terminological development

- **Propose initiatives to augment the CDE information model.** To succeed, terminologies must develop associated meta-knowledge and meta-data about each term to provide linkages between terms, logical contexts for terms, and specifications on instantiating and using terms to clarify interrelationships. The ORTS working group will propose initiatives to

- ✓ Describe the CDE database schema and information model in detail, for public review and comparison to other models and terminologies based on meta-data standards and in collaboration with ongoing efforts to harmonize medical standard repositories (HFCA's meta-data repository)
- ✓ Establish a rich, consistent information model for CDEs, by building on existing CDE "Categories" and ultimately employing knowledge representation techniques like semantic networks and description logic
- ✓ Create detailed data dictionary entries for new data elements, including non-textual data (e.g., imaging), to minimize variations

- **Recommend methods to encourage the dissemination and use of CDEs.** In the effort to establish CDEs as a *de facto* standard for oncology data collection, NCI now makes them available for free on its website. More work is needed to increase the use of CDEs in and outside of the cooperative groups. New functionalities are key to attracting additional researchers to use the CDEs and other CII technology. The ORTS working group meeting will identify approaches to
  - ✓ Enhance the web-enabled interface to CDEs, making it easier for new users and users outside the cooperative groups
  - ✓ Automate the connection between the CDE web site and research systems using CDEs, by encouraging projects at different phases of the cancer lifecycle to download and incorporate CDEs into data collection systems for clinical trials, possibly through funding supplements to existing trials
  - ✓ Enhance download formats, including case report form (CRF) templates, draft database designs, and XML, enabling users to search for and download relevant CDEs and evolving the CDE resource into a meta-data repository

Recommendation 3. **Focus informatics efforts on demonstration and evaluation projects that enhance NCI's ability to carry out its mission, by building on ongoing mainstream informatics initiatives and Internet technologies.**

Implementing the CII is a complex and long-term task, but most of the technologies and applications required to support it are available now. Creation of the CII requires a set of common infrastructure services, such as medical informatics standards and tools, digital libraries, collaboration tools, security services, and electronic transaction support.

In order to maximize impact in the NCI community, we recommend that the Director of the Office of Informatics exploit existing and emerging technologies and capitalize on initiatives underway outside the National Cancer Institute. The NCI operates in an environment of diverse stakeholders, rapidly evolving policy and technology, extensive interdependency with externally-developed informatics and Internet infrastructure, and long-lived data and processes associated with trials. In the overall process of developing the CII, we therefore recommend that the NCI fulfill three specific roles.

First, NCI is the principal stakeholder for the long-term interests of the cancer-trials community. NCI should therefore emphasize investments that address issues of future concern, such as

support for the evolution of standards, or consideration of issues relating to the scaling-up of the extent of CII deployment among the diverse participants in NCI activities. For example, when new standards are proposed (such as CDEs), the NCI should, from the outset, assure that the designs do not preclude smooth transitions to exploit anticipated future developments in health care and in information technology. In special cases, these investments can include generic information technologies that play a critical role in NCI infrastructure development. (It may be appropriate to co-manage these investments with other agencies that serve in a more primary role in technology-development.)

Second, NCI has a principal role in buying down the risks of creating and adopting new technologies. For example, NCI should make targeted investments to assist early adopters in evaluating CII technologies. NCI can also undertake targeted experiments to assess how new standards and processes may introduce or eliminate barriers to efficient trials management and broad participation.

Third, the NCI needs to make specific investments that address compelling nearer-term needs. This includes "bootstrapping" new efforts in the development of standards and technology. It is essential that these investments be made in a manner that is consistent with the long-term CII vision. This keeps the CII vision grounded in the baseline of present practice (and it may entail adapting the CII vision). By getting involved at very early stages, NCI can exert greater leverage with its investment. This approach assures that NCI informatics investment is consistent with overall strategy. Within the overall strategy, of course, there may be a need to explore diverse approaches to particular problems.

In carrying out these roles, the NCI Office of Informatics can maximize the return on its investment by leveraging ongoing informatics and Internet technology efforts to address NCI-specific needs. For example, CDE standards developed under NCI sponsorship should be integrated into mainstream framework efforts such as HL7.

As an example of successful mediation of community standards-development efforts, we note the work of the Internet Engineering Task Force (IETF), which has been the governing body for Internet standards since the early 1970s. The IETF has succeeded in building a national-scale community process to support an evolving collection of standards and capabilities. We recommend the IETF model because, in the rapidly evolving environment of cancer research and treatment, the only constant can be a set of principles that make up the process model:

- ✓ Provide mechanisms to facilitate stakeholder participation
- ✓ Leverage sponsorship rather than subsidize the entire CII
- ✓ Provide both a test bed and an infrastructure.

NCI should identify critical areas of standards and technology development in which it needs to participate in order to address the needs identified above. Standards development, in the IETF process, involves not only community consensus efforts, but also development of technology prototypes that can enable direct evaluation of candidate approaches to be undertaken.

With respect to standards, we advise Office of Informatics to undertake efforts such as

- **Collaborate with Radiology and Pathology to ensure that their efforts to create digital libraries for large-scale multimedia records are compatible with the CII.** Building on its success in persuading vendors to adopt the DICOM standard, the Radiological Society of North America is actively pursuing the multimedia record and the integration of imaging information into the clinical record. Pathology is pursuing similar efforts with tissue banks, with funding from NCI forthcoming for three to five institutions to develop shared tissue resources.
  www.nema.org/nema.dicom/
  www.rsna.org/REG/practiceres/mirc/mircindex.html
  www.rsna.org/IHE/ihe_index.html
  www.acrin.org

- **Participate in the Guidelines Interchange Format (GLIF) Workshop in March 2000 to draw upon and impact ongoing efforts to develop suites of building blocks**. This workshop includes multiple governmental sponsors along with the American College of Physicians-American Society of Internal Medicine. As such, it provides an opportunity to begin to consolidate the national cancer community and its diverse stakeholder groups in assessing current efforts (both intramural and extramural) and defining next steps.

- **Exploit e-commerce and emerging business models to support electronic transactions between parties.** Standard practices in e-commerce, notably business-to-business applications, have brought multiple legacy systems together. Similar mechanisms will enable basic researchers to collaborate with clinical researchers and result in the more effective use and re-use of knowledge in their own legacy systems. They will also allow for linkages with individuals and entities outside NCI, from patients to ancillary care providers.

With respect to technology development, we advise the Office of Informatics to undertake efforts such as:

- **Capitalize on work developing collaborative tools done by other federal agencies.** Issues surrounding scientific collaboration and research were recently explored at a workshop on Collaborative Problem Solving Environments, sponsored by the Department of Energy and attended by the NCI Office of Informatics. Their findings and work ongoing in the National Science Foundation and the Defense Applied Research Projects Agency should be analyzed for insight into issues central to the CII.
  www.emsl.pnl.gov:2080/docs/cpse/workshop/
  www.nci.nih.gov/dip/concepts.htm#c1

- **Exploit national initiatives to create security services needed to protect patient privacy and confidentiality.** Work by the Computer-Based Patient Record Institute (CPRI) and in conjunction with the Health Insurance Portability and Accountability Act (HIPAA) addresses the policy and technology issues critical to the CII and the patient-

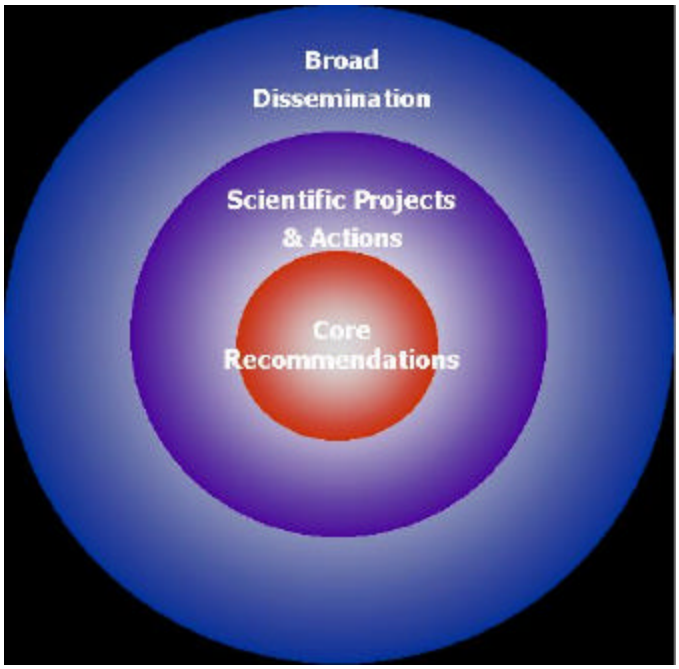
centric data it will include. The Office of Informatics should leverage this work rather than develop services independently.
www.cpri.org/resource/index.html
http://aspe.os.dhhs.gov/admnsimp/

Recommendation 4. **Develop a process to strategically and tactically diffuse the products and concepts of recommendations 1, 2, and 3 throughout the cancer community.**

In the cancer community there are a number of early adopters or visionaries of a comprehensive cancer informatics infrastructure and its potential impact on the clinical trials process. There is sometimes a "gap" between these early adopter/visionaries and the majority of others who are working in the cancer area. The goal of this recommendation is to develop systematic demonstration and evaluation efforts that will illustrate the impact to the people in the cancer community that can be called "early majority pragmatists."

We recommend a concentric circle model to demonstrate this change oriented diffusion process. The center circle within this model contains the three core product recommendations. The circle immediately touching the recommendations contains a number of specific projects and actions that are highly relevant to the current user community, e.g., Centers, groups, NCI, etc. To fulfill the demonstration effect of the items listed in this circle, people who are "early adopters" could be asked to complete demonstration projects. The types of items listed in the next concentric circle will be dissemination items to the people who are more conservative in their approach.

Figure 4: Dissemination Model



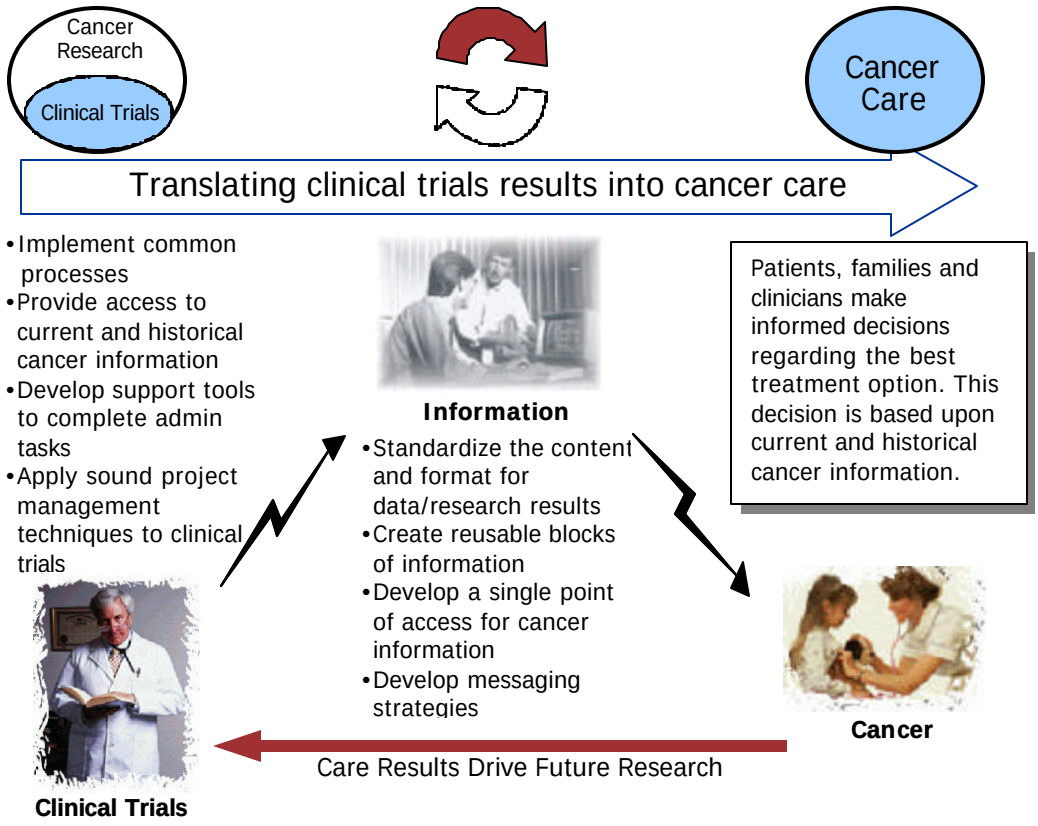
- **Convene a planning meeting/working group with the representation from the recommendation developers and early adopter/visionaries who are respected within NCI and within the cancer community.** During this meeting plot those efforts—along a time and the concentric model—that (1) are needed, (2) would demonstrate the impact of each of the recommendations in a CII enabled process, and (3) that would be implemented by people highly respected by NCI and the cancer community.

- **Develop the processes, identify and remove the barriers, and request the completion of the targeted diffusion efforts.** The planning/working group will be responsible for the components in this portion of the diffusion plan. We strongly suggest that the planning group consider tactics for disseminating information on the CII in NCI announcements, including RFAs.

FROM THEORY TO PRACTICE: CLINICAL TRIALS IN 2004

In 2004, the Cancer Informatics Infrastructure (CII) will translate clinical trials results into clinical care, and care results will drive future research. With common processes and tools in place, the CII will expedite information exchange. Access to information will support all stakeholders – patients and physicians, investigators, trial managers, and payers – as they make vital decisions affecting the course of cancer treatment and research. In the end, the benefits will accrue to the patient, and the NCI will realize its ultimate mission: to bring better care to the American public.

Figure 5: Cancer Care and Cancer Research in 2004



The information and knowledge depicted in Figure 5 will make it possible for

Patients and their physicians to
- ✓ Access up-to-date medical information
- ✓ Maintain patient-centric records
- ✓ Be partners in shared decision making.

Investigators to
- ✓ Design and obtain approval for a trial in 60 days
- ✓ Rapidly accrue patients into trials
- ✓ Populate research databases using clinical data.

Trial Managers to
- ✓ Minimize time from scientific concept to first patient accrual
- ✓ Maximize patient participation in cancer clinical trials
- ✓ Exchange information to optimize effective studies
- ✓ Facilitate translation of clinical trial results into cancer care.

Payers to
- ✓ Provide high quality cancer treatment for their members
- ✓ Make a solid business case for participating in clinical trials.

We believe that moving the CII from theory into practice will help the National Cancer Institute achieve its mission of lessening the burden of cancer for all Americans, and we urge the Director of the Office of Informatics to continue working towards the vision we have presented in this report.

APPENDICES

1. Long Range Planning Committee Membership and Meetings

2. Summaries and Scenarios

3. CDE Development Model: Spiral CT in Lung Cancer